

**The Claims:**

1. (Currently Amended) ~~A system for calculating a potential of mean force (PMF) score of a protein-ligand complex, the system~~ An apparatus comprising:

~~a repulsion term module that:~~

~~accesses one or more parameters useable to calculate a repulsion term useable to calculate a PMF of a protein-ligand atom pair in the protein-ligand complex, the one or more parameters corresponding to an atom-pair type of the protein-ligand atom pair;~~

~~using the one or more accessed parameters, calculates the repulsion term useable to calculate the PMF of the protein-ligand atom pair; and~~

~~communicates the calculated repulsion term for calculation of the PMF score of the protein-ligand complex.~~

~~one or more processors; and~~

~~a memory coupled to the processors comprising one or more instructions, the processors operable when executing the instructions to:~~

~~determine an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;~~

~~calculate a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type;~~

~~calculate a potential of mean force (PMF) of the protein-ligand atom pair according to the calculated repulsion term of the protein-ligand atom pair; and~~

~~calculate a PMF score of the protein-ligand complex according to the calculated PMF of the protein-ligand atom pair, the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex.~~

2. (Currently Amended) The system of Claim 1, wherein ~~one of the parameters corresponding to the atom-pair type of the protein-ligand atom pair comprises an empirically derived minimum binding-energy distance value corresponding to the atom-pair type of the protein-ligand atom pair~~ the minimum binding-energy distance value of the atom-pair type is an empirically derived minimum binding-energy distance value of the atom-pair type and the well-depth value of the atom-pair type is an empirically derived well-depth value of the atom-pair type.

3. (Canceled)

4. (Canceled)

5. (Currently Amended) The system of ~~Claim 4~~ Claim 2, wherein ~~a set of a plurality of empirically derived minimum binding energy distance and well depth values corresponding to a plurality of protein-ligand atom pairs comprises the empirically derived minimum binding energy distance and well depth values corresponding to the atom-pair type of the protein-ligand atom pair, the set of empirically derived minimum binding energy distance and well depth values yielding a best agreement with a plurality of actual analyzed protein-ligand atom pairs~~ a first set of empirically derived minimum binding-energy distances and well-depth values comprises the minimum binding-energy distance value and the well-depth value of the atom-pair type, the first set yielding a better agreement with a plurality of actual analyzed protein-ligand atom pairs than one or more second sets of empirically derived minimum binding-energy distances and well-depth values.

6. (Canceled)

7. (Currently Amended) The system of Claim 5, wherein ~~the best agreement between the set of empirically derived minimum binding energy distance and well depth values and the plurality of analyzed protein-ligand atom pairs is determined according to a plurality of root mean square (RMS) deviations between:~~

~~protein-ligand complex structures predicted according to the set of empirically derived minimum binding energy distance and well depth values; and~~

~~actual analyzed protein-ligand complex structures corresponding to the predicted protein-ligand complex structures;~~

root mean square (RMS) deviation between actual analyzed protein-ligand complex structures and protein-ligand complex structures predicted according to a set of empirically derived minimum binding-energy distances and well-depth values determines agreement between the set of empirically derived minimum binding-energy distances and well-depth values and the actual analyzed protein-ligand atom pairs.

8. (Canceled)

9. (Currently Amended) The system of ~~Claim 7~~ Claim 5, wherein one or more of the ~~plurality of sets of empirically derived minimum binding energy distance and well depth values are generated according to one or more of:~~

~~one or more manual processes; and~~

~~one or more automatic processes.~~

first set of empirically derived minimum binding-energy distances and well-depth values or second sets of empirically derived minimum binding-energy distances and well-depth values are each a product of one or more manual processes or automatic processes.

10. (Currently Amended) The system of Claim 9, wherein at least one of the automatic processes comprises execution of a genetic algorithm.

11. (Currently Amended) A ~~method for calculating a potential of mean force (PMF) score of a protein-ligand complex, the method comprising:~~

~~accessing one or more parameters useable to calculate a repulsion term useable to calculate a PMF of a protein-ligand atom pair in the protein-ligand complex, the one or more parameters corresponding to an atom-pair type of the protein-ligand atom pair;~~

~~using the one or more accessed parameters, calculating the repulsion term useable to calculate the PMF of the protein-ligand atom pair; and~~

~~communicating the calculated repulsion term for calculation of the PMF score of the protein-ligand complex.~~

determining an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

calculating a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type;

calculating a potential of mean force (PMF) of the protein-ligand atom pair according to the calculated repulsion term of the protein-ligand atom pair; and

calculating a PMF score of the protein-ligand complex according to the calculated PMF of the protein-ligand atom pair, the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex.

12. (Currently Amended) The method of Claim 11, wherein ~~one of the parameters corresponding to the atom-pair type of the protein-ligand atom pair comprises an empirically derived minimum binding-energy distance value corresponding to the atom-pair type of the protein-ligand atom pair~~ the minimum binding-energy distance value of the atom-pair type is an empirically derived minimum binding-energy distance value of the atom-pair type and the well-depth value of the atom-pair type is an empirically derived well-depth value of the atom-pair type.

13. (Canceled)

14. (Canceled)

15. (Currently Amended) The method of ~~Claim 14~~ Claim 12, wherein ~~a set of a plurality of empirically derived minimum binding-energy distance and well-depth values corresponding to a plurality of protein-ligand atom pairs comprises the empirically derived minimum binding-energy distance and well-depth values corresponding to the atom-pair type of the protein-ligand atom pair, the set of empirically derived minimum binding-energy distance and well-depth values yielding a best agreement with a plurality of actual analyzed protein-ligand atom pairs~~ a first set of empirically derived minimum binding-energy distances and well-depth values comprises the minimum binding-energy distance value and the well-depth value of the atom-pair type, the first set yielding a better agreement with a plurality of actual analyzed protein-ligand atom pairs than one or more second sets of empirically derived minimum binding-energy distances and well-depth values.

16. (Canceled)

17. (Currently Amended) The method of Claim 15, wherein ~~the best agreement between the set of empirically derived minimum binding energy distance and well depth values and the plurality of analyzed protein ligand atom pairs is determined according to a plurality of root mean square (RMS) deviations between:~~

~~protein ligand complex structures predicted according to the set of empirically derived minimum binding energy distance and well depth values; and~~

~~actual analyzed protein ligand complex structures corresponding to the predicted protein ligand complex structures.~~

root mean square (RMS) deviation between actual analyzed protein-ligand complex structures and protein-ligand complex structures predicted according to a set of empirically derived minimum binding-energy distances and well-depth values determines agreement between the set of empirically derived minimum binding-energy distances and well-depth values and the actual analyzed protein-ligand atom pairs.

18. (Canceled)

19. (Currently Amended) The method of ~~Claim 17~~ Claim 5, wherein one or more of the ~~plurality of sets of empirically derived minimum binding energy distance and well depth values are generated according to one or more of:~~

~~one or more manual processes; and~~

~~one or more automatic processes.~~

first set of empirically derived minimum binding-energy distances and well-depth values or second sets of empirically derived minimum binding-energy distances and well-depth values are each a product of one or more manual processes or automatic processes.

20. (Currently) The method of Claim 19, wherein at least one of the automatic processes comprises execution of a genetic algorithm.

21. ~~(Currently Amended) Software for calculating a potential of mean force (PMF) score of a protein-ligand complex, the software embodied in computer-readable Logic encoded in one or more media for execution and when executed operable to:~~

~~access one or more parameters useable to calculate a repulsion term useable to calculate a PMF of a protein-ligand atom pair in the protein-ligand complex, the one or more parameters corresponding to an atom-pair type of the protein-ligand atom pair;~~

~~using the one or more accessed parameters, calculate the repulsion term useable to calculate the PMF of the protein-ligand atom pair; and~~

~~communicate the calculated repulsion term for calculation of the PMF score of the protein-ligand complex.~~

determine an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

calculate a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type;

calculate a potential of mean force (PMF) of the protein-ligand atom pair according to the calculated repulsion term of the protein-ligand atom pair; and

calculate a PMF score of the protein-ligand complex according to the calculated PMF of the protein-ligand atom pair, the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex.

22. (Currently Amended) The ~~software~~ logic of Claim 21, wherein ~~one of the parameters corresponding to the atom-pair type of the protein-ligand atom pair comprises an empirically derived minimum binding-energy distance value corresponding to the atom-pair type of the protein-ligand atom pair. the minimum binding-energy distance value of the atom-pair type is an empirically derived minimum binding-energy distance value of the atom-pair type and the well-depth value of the atom-pair type is an empirically derived well-depth value of the atom-pair type.~~

23. (Canceled)

24. (Canceled)

25. (Currently Amended) The software logic of ~~Claim 24~~ Claim 22, wherein ~~a set of a plurality of empirically derived minimum binding-energy distance and well-depth values corresponding to a plurality of protein-ligand atom pairs comprises the empirically derived minimum binding-energy distance and well-depth values corresponding to the atom-pair type of the protein-ligand atom pair, the set of empirically derived minimum binding-energy distance and well-depth values yielding a best agreement with a plurality of actual analyzed protein-ligand atom pairs.~~ a first set of empirically derived minimum binding-energy distances and well-depth values comprises the minimum binding-energy distance value and the well-depth value of the atom-pair type, the first set yielding a better agreement with a plurality of actual analyzed protein-ligand atom pairs than one or more second sets of empirically derived minimum binding-energy distances and well-depth values.

26. (Canceled)

27. (Currently Amended) The software logic of Claim 25, wherein ~~the best agreement between the set of empirically derived minimum binding-energy distance and well-depth values and the plurality of analyzed protein-ligand atom pairs is determined according to a plurality of root mean square (RMS) deviations between:~~

~~protein-ligand complex structures predicted according to the set of empirically derived minimum binding-energy distance and well-depth values; and~~

~~actual analyzed protein-ligand complex structures corresponding to the predicted protein-ligand complex structures.~~

root mean square (RMS) deviation between actual analyzed protein-ligand complex structures and protein-ligand complex structures predicted according to a set of empirically derived minimum binding-energy distances and well-depth values determines agreement between the set of empirically derived minimum binding-energy distances and well-depth values and the actual analyzed protein-ligand atom pairs.

28. (Canceled)

29. (Currently Amended) The ~~software logic of Claim 27~~ Claim 25, wherein one or more of the ~~plurality of sets of empirically derived minimum binding-energy distance and well-depth values are generated according to one or more of:~~

~~one or more manual processes; and~~

~~one or more automatic processes.~~

first set of empirically derived minimum binding-energy distances and well-depth values or second sets of empirically derived minimum binding-energy distances and well-depth values are each a product of one or more manual processes or automatic processes.

30. (Currently Amended) The ~~software logic of Claim 29~~, wherein at least one of the automatic processes comprises execution of a genetic algorithm.

31. (Currently Amended) A system ~~for calculating a potential of mean force (PMF) score of a protein-ligand complex, the system comprising:~~

~~means for accessing one or more parameters useable to calculate a repulsion term useable to calculate a PMF of a protein-ligand atom pair in the protein-ligand complex, the one or more parameters corresponding to an atom-pair type of the protein-ligand atom pair;~~

~~means for, using the one or more accessed parameters, calculating the repulsion term useable to calculate the PMF of the protein-ligand atom pair; and~~

~~means for communicating the calculated repulsion term for calculation of the PMF score of the protein-ligand complex.~~

means for determining an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;

means for calculating a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type;

means for calculating a potential of mean force (PMF) of the protein-ligand atom pair according to the calculated repulsion term of the protein-ligand atom pair; and

means for calculating a PMF score of the protein-ligand complex according to the calculated PMF of the protein-ligand atom pair, the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex.